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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/696,909	10/29/2003	James B. Lorens	7946-79836-01	9257
74839	7590			
Klarquist Sparkman, LLP				
121 SW Salmon St				
Suite 1600				
Portland, OR 97204				
05/27/2010				
EXAMINER				
REDDIG, PETER J				
ART UNIT		PAPER NUMBER		
1642				
NOTIFICATION DATE		DELIVERY MODE		
05/27/2010		ELECTRONIC		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary

Application No.

10/696,909

Applicant(s)

LORENS ET AL.

Examiner

Peter J. Reddig

Art Unit

1642

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 May 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 12, 14-18, 27, 41-44 and 54-63 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 12, 14-18, 27, 41-44 and 54-63 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-506)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ ~~Notice of Informal Patent Application~~
- 6) ☐ Other: _____

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114 was filed in this application after a decision by the Board of Patent Appeals and Interferences, but before the filing of a Notice of Appeal to the Court of Appeals for the Federal Circuit or the commencement of a civil action. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 05/12/2010 has been entered.

2. Claims 1, 12, 14-18, 27, 41-44, and 54-63 are currently pending and under examination.

New Grounds of Rejection

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

3. Claims 27 and 54 are rejected under 35 U.S.C. 102(b) as being anticipated by
O'Donnell et al. (Am. J. Path. 1999, 154: 1171-1180, IDS item).

O'Donnell et al. teach treating human endothelial cells (HUVEC) expressing Axl polypeptide with TNF α in a cell assay for the viability of the endothelial cell. O'Donnell et al. teach that TNF α inhibits the viability of the HUVECs in the absence and presence of GAS6. See Abstract, p. 1175-1176 and ¶ bridging p. 1178-1179, and Fig. 7 and 8. Thus, O'Donnell et al. identifies TNF α as a compound that inhibits the viability of HUVECs, an angiogenesis phenotype in the cell based assay, and, inherently, identifies a compound that inhibits angiogenesis.

Given, that the cells express wild type human Axl, the Axl cells would inherently comprise an amino acid sequence greater than about 95% identity to full length SEQ ID NO: 4, see Appendix 1 and have kinase activity in the absence of TNF α . The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the method of the prior art does not possess the same material, structural and functional characteristics of the claimed method. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed method is different from those taught by the prior art and to establish patentable differences. See *In re Best* 562F.2d 1252, 195 USPQ 430 (CCPA 1977).

It is noted that although the Axl in HUVECs (see Fig. 3), is not a recombinant Axl, the prior art Axl functions in the same manner as the claimed recombinant Axl. Furthermore, "recombinant Axl" merely implies a method of production of Axl and the patentability of a product is determined by the novelty and nonobviousness of the claimed product itself without consideration of the process for making it which is recited in the claim. See *In re Thorpe*, 227 USPQ 964 (Fed. Cir. 1985).

3. Claims 1, 14, 15, 16, 18, 27, 41, 42, 44, 54, 55, 56-58, 60, and 61 are rejected under 35 U.S.C. 102(c) as being anticipated by Mor, O. (US Pat. App. Pub. 2003/0157573 A1 Feb. 12, 2002).

Mor teaches identifying an inhibitor Axl by determining the ability of compounds such as antibodies, antisense molecules, and small organic molecules to inhibit the Axl kinase activity in cells, like endothelial cells, expressing endogenous or human Axl, which comprises SEQ ID NO: 4, determining the inhibition of Axl kinase activity *in vitro*, and by determining cell survival, cell differentiation, or cell proliferation response to the compound. See claims 1-19, 21-23, and 35, Abstract, ¶ 0020, 0022, 0033-0036, 0045, 0046, 0049-0064, 0108, 0249, 0255, and Appendix 1 and 2. Mor teaches determining decreases in expression of the Axl polypeptide in response to the compounds. See ¶ 0065. Mor teaches that the identified drugs may be used as anti-angiogenic drugs for the treatment of cancer by preventing or reducing the proliferation of endothelial cells. See ¶ 0090.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 12, 17, 43, 59, 62, and 63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mor, O. (US Pat. App. Pub. 2003/0157573 A1 Feb. 12, 2002) as applied to claims, 1 14, 15, 16, 18, 27, 41, 42, 44, 54, 55, 56-58, 60, and 61 above, further in view of Klinghoffer et al. (United States Patent Application Publication No.: 2004/0077574, May 23, 2002, previously cited), further in view of O'Donnell et al. (Am. J. Path. 1999, 154: 1171-1180, IDS item), and, further in view of Varner and Cheresh (Current Opinion in Cell Biology, October 1996, 8:724-730, previously cited).

Mor teaches as set forth above, and teaches that activation of Axl increases the survival of endothelial cells and induces migration of vascular muscle cells, but does not specifically teach using RNAi as a compound or assaying α V β 3 expression, tube formation, or haptotaxis.

Klinghoffer et al. teach that siRNA/RNAi polynucleotides offer advantages over other types of polynucleotides for sequence specific alteration of gene expression including lower effective siRNA/RNAi polynucleotide concentration, enhance stability, shorter lengths, they are

readily taken up by intact cells, and are effective at concentration that are several orders of magnitude lower than those required for either antisense or ribozyme polynucleotides, see paragraph 0022 and 0025.

O'Donnell et al. teach that Axl exhibits homophilic binding via its extracellular domain, which could be relevant to tube formation in angiogenesis. See p. 1176-2nd col. O'Donnell et al. teach that the ligand of Axl, Gas6, has multiple properties relevant to vascular biology including promoting adhesion of Axl expressing cells and stimulation of chemotaxis of vascular smooth muscle cells. See p. 1177-2nd col.

Varner and Cheresh teach that integrin $\alpha V\beta 3$ is significantly upregulated on vascular cells within human tumors and in response to growth factors and plays a biological role in a critical event of blood vessel formation during tumor angiogenesis by promoting vascular cell survival and that inhibition of $\alpha V\beta 3$ inhibits angiogenesis, see section on Role of Integrins in Tumor Angiogenesis, p. 726- 727.

It would have been *prima facie* obvious at the time the invention was made to combine teachings of Mor and Klinghoffer et al. and use RNAi molecules in the screening methods of Mor because Klinghoffer et al. teach the advantages of siRNA as inhibitory molecules and one would have been motivated to identify the most effective inhibitory molecule in the screens of Mor to identify the most effective anti-angiogenic drug. Given that screening assays are routinely performed in the art, one of skill in the art would have a reasonable expectation of success of making and using the claimed assay.

Additionally, it would have been *prima facie* obvious at the time the invention was made to combine teachings of Mor, O'Donnell et al., and Varner and Cheresh and measure $\alpha V\beta 3$

expression or tube formation in endothelial cells in response to the test compounds because Mor teaches assaying cellular differentiation in the screening assays for identifying angiogenesis inhibitors, O'Donnell et al. teaches that Axl may be involved in tube formation during and angiogenesis, and Varner and Cheresch teach that $\alpha V\beta 3$ expression plays a critical role in blood vessel formation during tumor angiogenesis, $\alpha V\beta 3$ is important for endothelial cell survival (like Axl), and inhibition of $\alpha V\beta 3$ inhibits angiogenesis.

5. All other rejections set forth in the Office Action of 06/23/2008 are withdrawn.
6. No claims allowed.
7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter J. Reddig whose telephone number is (571)272-9031. The examiner can normally be reached on M-F 8:30 a.m.-5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Helms Larry can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Peter J Reddig/
Primary Examiner, Art Unit 1642

Art Unit: 1642

Appendix 1, Alignment of SEQ ID NO: 4 and Human AXL
 US-08-372-892-2
 ; Sequence 2, Application US/08372892
 ; Patent No. 5468634
 ; GENERAL INFORMATION:
 ; APPLICANT: Liu, Edison T.
 ; TITLE OF INVENTION: AXL Oncogene
 ; NUMBER OF SEQUENCES: 6
 ; CORRESPONDENCE ADDRESS:
 ; ADDRESSEE: Kenneth D. Sibley; Bell, Seltzer, Park and
 ; ADDRESSEE: Gibson
 ; STREET: Post Office Drawer 34009
 ; CITY: Charlotte
 ; STATE: No. 5468634th Carolina
 ; COUNTRY: U.S.A.
 ; ZIP: 28234
 ; COMPUTER READABLE FORM:
 ; MEDIUM TYPE: Floppy disk
 ; COMPUTER: IBM PC compatible
 ; OPERATING SYSTEM: PC-DOS/MS-DOS
 ; SOFTWARE: PatentIn Release #1.0, Version #1.25
 ; CURRENT APPLICATION DATA:
 ; APPLICATION NUMBER: US/08/372,892
 ; FILING DATE:
 ; CLASSIFICATION: 435
 ; PRIOR APPLICATION DATA:
 ; APPLICATION NUMBER: US/07/718,572
 ; FILING DATE:
 ; ATTORNEY/AGENT INFORMATION:
 ; NAME: Sibley, Kenneth D.
 ; REGISTRATION NUMBER: 31,665
 ; REFERENCE/DOCKET NUMBER: 5470-15
 ; TELECOMMUNICATION INFORMATION:
 ; TELEPHONE: 919-881-3140
 ; TELEFAX: 919-881-3175
 ; TELEX: 575102
 ; INFORMATION FOR SEQ ID NO: 2:
 ; SEQUENCE CHARACTERISTICS:
 ; LENGTH: 894 amino acids
 ; TYPE: amino acid
 ; TOPOLOGY: linear
 ; MOLECULE TYPE: protein
 US-08-372-892-2

Query Match	100.0%;	Score 4793;	DB 1;	Length 894;
Best Local Similarity	100.0%;			
Matches	894;	Conservative	0;	Mismatches 0;
		Indels	0;	Gaps 0;

Qy	1	MAWRCPRMGRVPLAWCLALCGWACMAPRGTOAEESPFVGNPGNITGARGLTGTLRCQLQV	60
Db	1	MAWRCPRMGRVPLAWCLALCGWACMAPRGTOAEESPFVGNPGNITGARGLTGTLRCQLQV	60
Qy	61	QGEPEVHWLRDGGQILELADSTQTQVPLGEDEQDDWIVVSQRLRITSLQLSDTGQYQCILVF	120
Db	61	QGEPEVHWLRDGGQILELADSTQTQVPLGEDEQDDWIVVSQRLRITSLQLSDTGQYQCILVF	120
Qy	121	LGHQTFVSPQGYVGLGLELPYLEEPEDRTVAANTPFHLSCQAQGPPEVDLLWLQDAVPL	180
Db	121	LGHQTFVSPQGYVGLGLELPYLEEPEDRTVAANTPFHLSCQAQGPPEVDLLWLQDAVPL	180

Appendix 2
Alignment of SEQ ID NO: 4
US-10-365-135-2
; Sequence 2, Application US/10365135
; Publication No. US2003015753A1
; GENERAL INFORMATION:
; APPLICANT: Mor, Orna
; TITLE OF INVENTION: Use of the AXL Receptor For Diagnosis and Treatment of Renal
Disease
; FILE REFERENCE: 66781-A
; CURRENT APPLICATION NUMBER: US/10/365.135

Art Unit: 1642

; CURRENT FILING DATE: 2003-02-12
 ; NUMBER OF SEQ ID NOS: 6
 ; SOFTWARE: PatentIn version 3.2
 ; SEQ ID NO 2
 ; LENGTH: 894
 ; TYPE: PRT
 ; ORGANISM: Homo sapiens
 US-10-365-135-2

Query Match 99.7%; Score 4777; DB 4; Length 894;
 Best Local Similarity 99.7%; Pred. No. 7.5e-254;
 Matches 891; Conservative 1; Mismatches 2; Indels 0; Gaps 0;

Qy	1	MAWRCPRMGRVPLAWCLALCGWACMAFRGTQAEESPFVGNFGNITGARGLTGTLRCQLQV	60
Db	1	MAWRCPRMGRVPLAWCLALCGWACMAFRGTQAEESPFVGNFGNITGARGLTGTLRCQLQV	60
Qy	61	QGEPEVHWLRDGGQILELADSTQTQVPLGEDEQDDWIVVSQRLRITSLQSDTGOYQCLVF	120
Db	61	QGEPEVHWLRDGGQILELADSTQTQVPLGEDEQDDWIVVSQRLRITSLQSDTGOYQCLVF	120
Qy	121	LGHQTFVSPGVGLEGLPYFLEEPEDRTVAANTPFNLSCQAQGPPEVDLLWLQDAVPL	180
Db	121	LGHQTFVSPGVGLEGLPYFLEEPEDRTVAANTPFNLSCQAQGPPEVDLLWLQDAVPL	180
Qy	181	ATAPGHGQPSRLHVPGLNKTSSFSCEAHNAKGVTTSRTATITVLPQQPNLHLVSRQPT	240
Db	181	ATAPGHGQPSRLHVPGLNKTSSFSCEAHNAKGVTTSRTATITVLPQQPNLHLVSRQPT	240
Qy	241	LEVANTPGLSGIYPLTHCTLQAVLSDDGMGIQAGEPDPPPEEPLTSQASVPPHQLRLGSLH	300
Db	241	LEVANTPGLSGIYPLTHCTLQAVLSDDGMGIQAGEPDPPPEEPLTSQASVPPHQLRLGSLH	300
Qy	301	PHTPHYRIVACTSSQGPSSWTHWLPVETPEGVPLGPPENISATRNQSAQFVHWQEPRAPL	360
Db	301	PHTPHYRIVACTSSQGPSSWTHWLPVETPEGVPLGPPENISATRNQSAQFVHWQEPRAPL	360
Qy	361	QGTLLGRLAYQGQDTPFVLMIDIGLRQEVTLLEQGDGGSVSNLTVCVAAAYTAAGDGFWSLP	420
Db	361	QGTLLGRLAYQGQDTPFVLMIDIGLRQEVTLLEQGDGGSVSNLTVCVAAAYTAAGDGFWSLP	420
Qy	421	VPLEAWRPGEAQPVHQLVKEPSTPAFSPWVWVYLLGAVVAAACVLILALFLVHRRKKETR	480
Db	421	VPLEAWRPGEAQPVHQLVKEPSTPAFSPWVWVYLLGAVVAAACVLILALFLVHRRKKETR	480
Qy	481	YGEVFTEPTVERGELVVRYRVRKYSRRTTEATLNSLGISEELKEKLRDVMVDRHKVALGK	540
Db	481	YGEVFTEPTVERGELVVRYRVRKYSRRTTEATLNSLGISEELKEKLRDVMVDRHKVALGK	540
Qy	541	TLGEGFEGAVMEGQLNQDDSLKLVAVKTMKIAICTRSELEDPLSEAVCMKEFDPHPVNMRL	600
Db	541	TLGEGFEGAVMEGQLNQDDSLKLVAVKTMKIAICTRSELEDPLSEAVCMKEFDPHPVNMRL	600
Qy	601	IGVCFQGSERESFPAPVVILPFMKHGDLSFLYSRLGDQPVYLLPTQMLVKFMADIASGM	660
Db	601	IGVCFQGSERESFPAPVVILPFMKHGDLSFLYSRLGDQPVYLLPTQMLVKFMADIASGM	660
Qy	661	EYLSKTRFIHRDLAARNCMLNENMSVCVADFGLSKKIYNGDYRQGIARIKMPVKWIAIES	720
Db	661	EYLSKTRFIHRDLAARNCMLNENMSVCVADFGLSKKIYNGDYRQGIARIKMPVKWIAIES	720

Art Unit: 1642

Qy 721 LADRVYTSKSDVWSFGVTMWEIATRGTPTYPGVENSEIYDYLRQGNRLKQPADCLDGLYA 780
|||||
Db 721 LADRVYTSKSDVWSFGVTMWEIATRGTPTYPGVENSEIYDYLRQGNRLKQPADCLDGLYA 780
|||||

Qy 781 LMSRCWELNFPQDRPSFTELREDLENTLKLPPAQEPDEILYVNMDEGGGYPEPPGAAGGA 840
|||||
Db 781 LMSRCWELNFPQDRPSFTELREDLENTLKLPPAQEPDEILYVNMDEGGGYPEPPGAAGGA 840
|||||

Qy 841 DPPTQDPDKDSCSLTAAEVHPAGRYVLCPSSTTPSPAQPADRGSPAAPGQEDGA 894
|||||
Db 841 DPPTQDPDKDSCSLTAAEVHPAGRYVLCPSSTTPSPAQPADRGSPAAPGQEDGA 894
|||||